

Discussion:

Table 3 shows that A, B, C, and D produce similar degrees of IOP reduction with 0.3 μ g doses; however, E is essentially inactive at this dose.

In Table 4, it is apparent that the IOP reduction with 1 μ g of A is greater than that produced by 0.3 μ g of A, and the response to either of these doses of A is greater than the maximum reduction produced by either dose of E. These observations indicate that A (cloprostenol, isopropyl ester) is both more potent and produces a greater maximum response for IOP reduction than E (13, 14-dihydro-17-phenyl- 18, 19,20-trinor PGF_{2 α}).

EXAMPLE 3

The following Formulations 1-4 are representative pharmaceutical compositions of the invention for topical use in lowering of intraocular pressure. Each of Formulations 1 through 4 may be formulated in accordance with procedures known to those skilled in the art.

FORMULATION 1

| Ingredient | Amount (wt %) |
|---|---------------|
| (I), R ¹ = CH(CH ₃) ₂ ; R ² = Cl | 0.002 |
| Dextran 70 | 0.1 |
| Hydroxypropyl methylcellulose | 0.3 |
| Sodium Chloride | 0.77 |
| Potassium chloride | 0.12 |
| Disodium EDTA (Edetate disodium) | 0.05 |
| Benzalkonium chloride | 0.01 |
| HCl and/or NaOH | pH 7.2-7.5 |
| Purified water | q.s. to 100% |

FORMULATION 2

| Ingredient | Amount (wt %) |
|--|---------------|
| (I), R ¹ = C(CH ₃) ₃ ; R ² = Cl | 0.01 |
| Monobasic sodium phosphate | 0.05 |
| Dibasic sodium phosphate (anhydrous) | 0.15 |
| Sodium chloride | 0.75 |
| Disodium EDTA (Edetate disodium) | 0.01 |
| Benzalkonium chloride | 0.02 |
| Polysorbate 80 | 0.15 |
| HCl and/or NaOH | pH 7.3-7.4 |
| Purified water | q.s. to 100% |

FORMULATION 3

| Ingredient | Amount (wt %) |
|---|---------------|
| (I), R ¹ = CH ₃ ; R ² = Cl | 0.001 |
| Dextran 70 | 0.1 |
| Hydroxypropyl methylcellulose | 0.5 |
| Monobasic sodium phosphate | 0.05 |
| Dibasic sodium phosphate (anhydrous) | 0.15 |
| Sodium chloride | 0.75 |
| Disodium EDTA (Edetate disodium) | 0.05 |
| Benzalkonium chloride | 0.01 |
| NaOH and/or HCl | pH 7.3-7.4 |
| Purified water | q.s. to 100% |

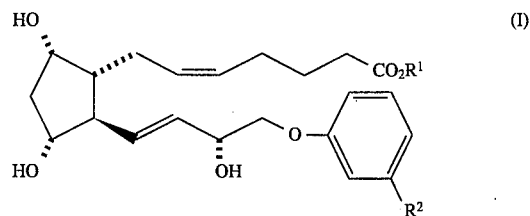
FORMULATION 4

| Ingredient | Amount (wt %) |
|---|---------------|
| (I), R ¹ = CH ₂ CH ₃ ; R ² = Cl | 0.003 |
| Monobasic sodium phosphate | 0.05 |
| Dibasic sodium phosphate (anhydrous) | 0.15 |
| Sodium chloride | 0.75 |
| Disodium EDTA (Edetate disodium) | 0.05 |
| Benzalkonium chloride | 0.01 |
| HCl and/or NaOH | pH 7.3-7.4 |
| Purified water | q.s. to 100% |

The invention has been described by reference to certain preferred embodiments; however, it should be understood that it may be embodied in other specific forms or variations thereof without departing from its spirit or essential characteristics. The embodiments described above are therefore considered to be illustrative in all respects and not restrictive, the scope of the invention being indicated by the appended claims rather than by the foregoing description.

What is claimed is:

1. A method of treating glaucoma and ocular hypertension which comprises topically administering to the affected eye a therapeutically effective amount of a compound of formula:



wherein: R¹=hydrogen, a cationic salt moiety, a pharmaceutically acceptable amine moiety or C₁-C₁₂ alkyl, cycloalkyl or aryl; and R²=Cl or CF₃.

2. The method of claim 1, wherein R¹ is selected from the group consisting of H, CH₃, CH(CH₃)₂ and C(CH₃)₃.

3. The method of claim 1, wherein R¹ is selected from the group consisting of Na⁺ and CH₃N⁺(CH₂OH)₃.

4. The method of claim 1, wherein R² is Cl.

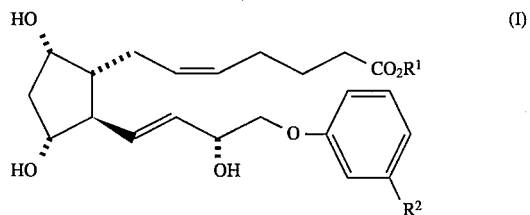
5. The method of claim 1, wherein R² is CF₃.

6. The method of claim 1, wherein between about 0.001 and about 1000 μ g/eye of a compound of formula (I) is administered.

7. The method of claim 6, wherein between about 0.01 and about 100 μ g/eye of a compound of formula (I) is administered.

8. The method of claim 6, wherein between about 0.05 and about 10 μ g/eye of a compound of formula (I) is administered.

9. A topical ophthalmic composition for the treatment of glaucoma and ocular hypertension in primates, comprising a therapeutically effective amount of a compound of formula:



wherein: R¹=hydrogen, a cationic salt moiety, a pharmaceutically acceptable amine moiety or C₁-C₁₂ alkyl, cycloalkyl